

Diabetes Mellitus

Part I (Introduction)



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تحذير هام

هذا الفيديو و جميع الرسوم التوضيحية المتاحة فى هذا الموقع هم تحت حماية قانون الملكية الفكرية

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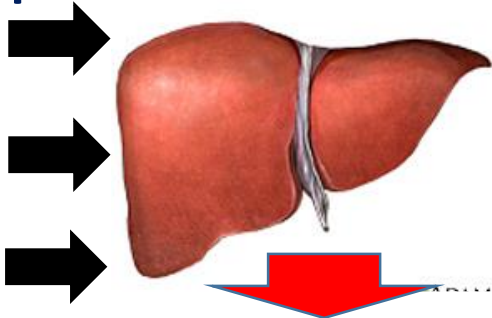
Diabetes Mellitus

Definition

Diabetes Mellitus is a chronic metabolic syndrome characterized by hyperglycemia and other metabolic derangements. The problem is caused by deficiency or diminished action of Insulin Hormone.

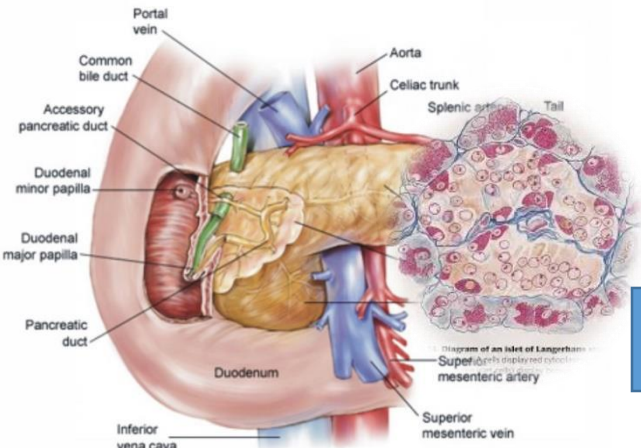
- ① Failure of β cells of the pancreas to produce Insulin (Type 1 DM)
- ② Insulin receptor defect (Type 2 DM)
- ③ Increase in Anti-Insulin hormones
- ④ Damage of the pancreas such as in Hemochromatosis, pancreatic cancer, and pancreatic removal.

- 1- Acromegaly
- 2- Pheochromocytoma
- 3- Cushing Syndrome



Glucose

Type 2 Diabetes



Pancreatic damage

Insulin

Type I Diabetes

Type I

- ① This type of DM typically occurs in young age
- ② It is due to absolute **insulin deficiency** due to destruction of β cells of the pancreas
- ③ Because Insulin levels are very low in this condition, the patient is more liable to the development of DKA
- ④ The condition is most likely caused by an environmental factor (e.g. virus) that causes injury to β cells. The damage of β cells causes release of its antigens which stimulate the production of autoantibodies that ultimately destroys all β cells.
- ⑤ Anti-Insulin Antibodies are usually present

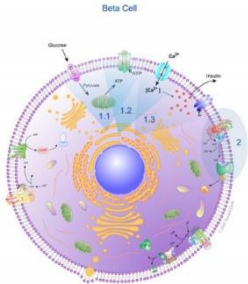
Chromosome

11

HLA

Environmental Factor

- 1- **Viruses** (e.g. Mumps- **Coxsackie Virus** (24 amino acids mimic GAD of pancreatic beta cells))
- 2- Vacor
- 3- Hydrogen Peroxide



- 1- Leak of β cell proteins leads to antibody formation (most against GAD)
- 2- Molecular mimicry with the virus
- 3- Expression of class II HLA (considered Non-Self)

Islet cell antibodies

DQ w7 (3.1): PROTECTS
DQw8 (3.2): MAXIMUM
RISK

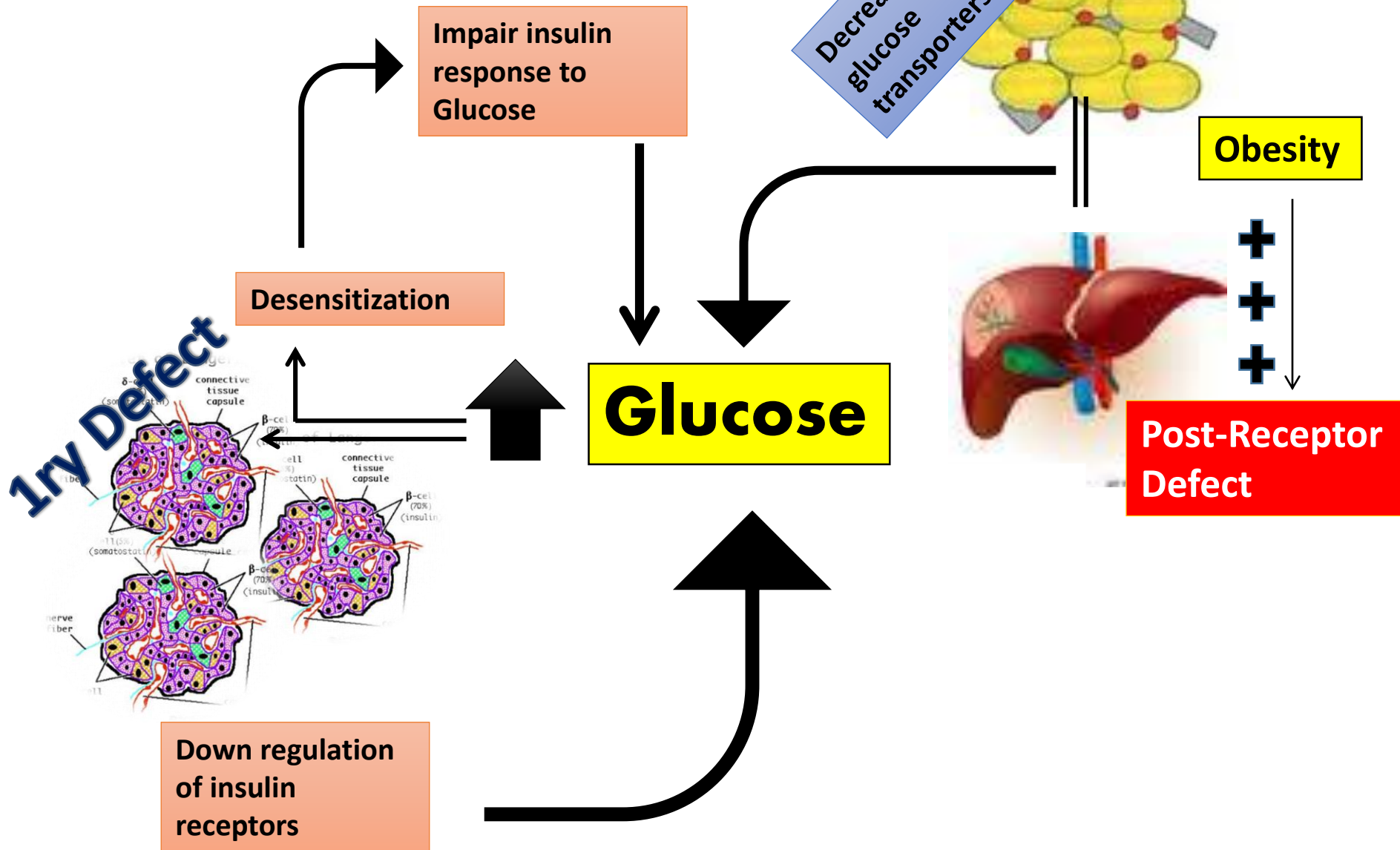
Humeral Immunity

Cell mediated immunity

Type 2

- ① This type of DM typically occurs in old age
- ② The primary defect in this problem is at the receptor level (**Post-Receptor Defect**)
- ③ The defect impairs insulin action and results in Hyperglycemia.
The pancreas reacts to this by increasing its insulin production as an attempt to lower the blood glucose levels (for this reason Insulin levels are usually high –or normal in type 2 DM)
- ④ Because insulin levels (unlike type 1 DM) are **NOT** very low (the patient usually does not develop DKA).
- ⑤ Obesity increases the Post-Receptor defect and thus aggravates the condition (Most patients are not obese)

Genetic?!

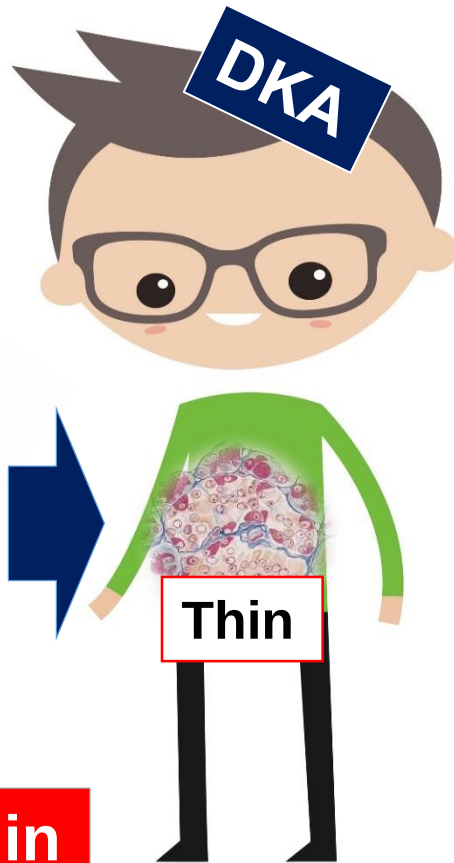


Type 1 DM

Anti-Insulin Antibodies

DKA

↓ Insulin



↑
ttt by Insulin

Type 2 DM

Insulin resistance

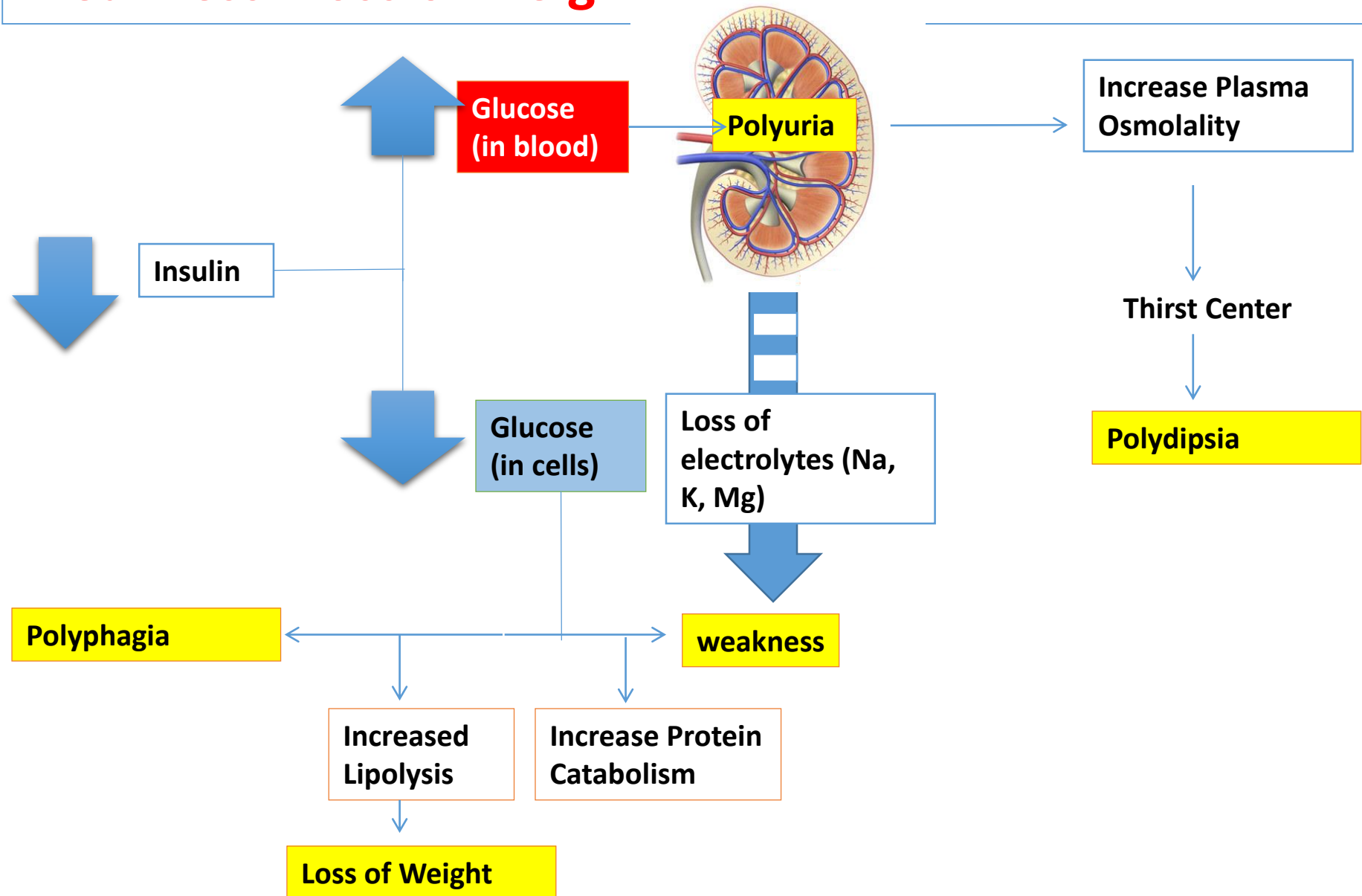
↑ Insulin



Diet Plus Oral
Hypoglycemic
drugs



Clinical picture: Polyuria-Polydipsia- Polyphagia- Weakness- Loss of weight.



Diagnostic Criteria of DM

	Normal	IGT	DM
① FPG (mg/dL)	< 100	100-125	≥ 126
② 2hs after glucose load (mg/dL)	< 140	≥ 140-199	≥ 200
③ HbA1c%	< 5.7	5.7-6.4	≥ 6.5

A fasting plasma glucose > 126 mg/dl or HbA1c of > 6.5% is diagnostic of DM if confirmed by repeated testing

Diabetes Mellitus

Part II (Complications)



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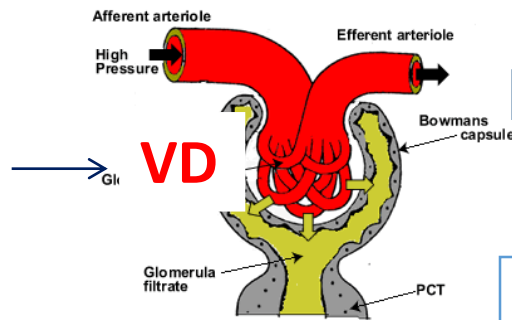


1 Decrease in contractile ability of meningeal cells

2 Immune Dysfunction

3 Non enzymatic glycosylation of proteins

4 Exceeded the capacity of glycolysis



GFR

Pathogenesis of DM

Infections

AGEs

Impair interaction between lamina propria and proteoglycans

Irreversible cross linkage to LDL

Irreversible cross linkage to Albumin

Increase capillary permeability

Proteinuria

Atherosclerosis

Attached to collagen in vessel wall

Thick capillary BM

Microangiopathy

Interact with specific receptors on Macrophages

**IL1
TNF**

Retinopathy

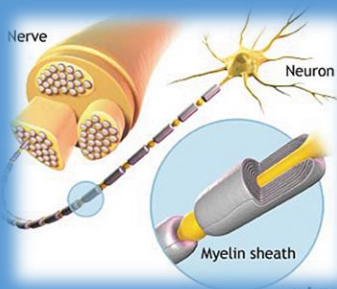
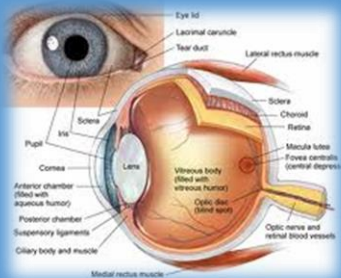
Neuropathy

Polyol pathway

Sorbitol

Eye damage

The presence of microangiopathy, neuropathy, and metabolic derangements in diabetic patients makes them liable to develop many complications.



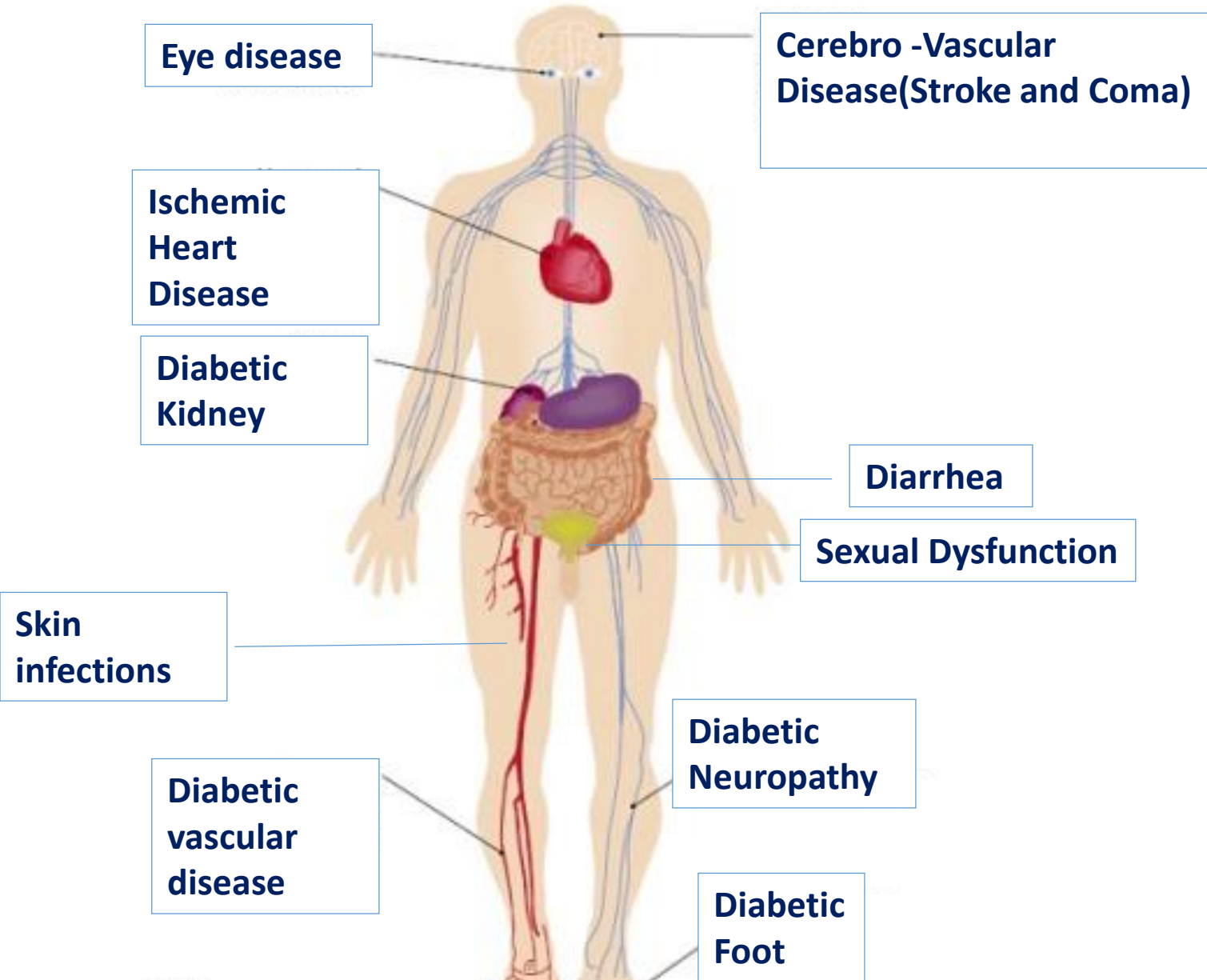
The most prominent complications of DM are:

1-Diabetic eye disease

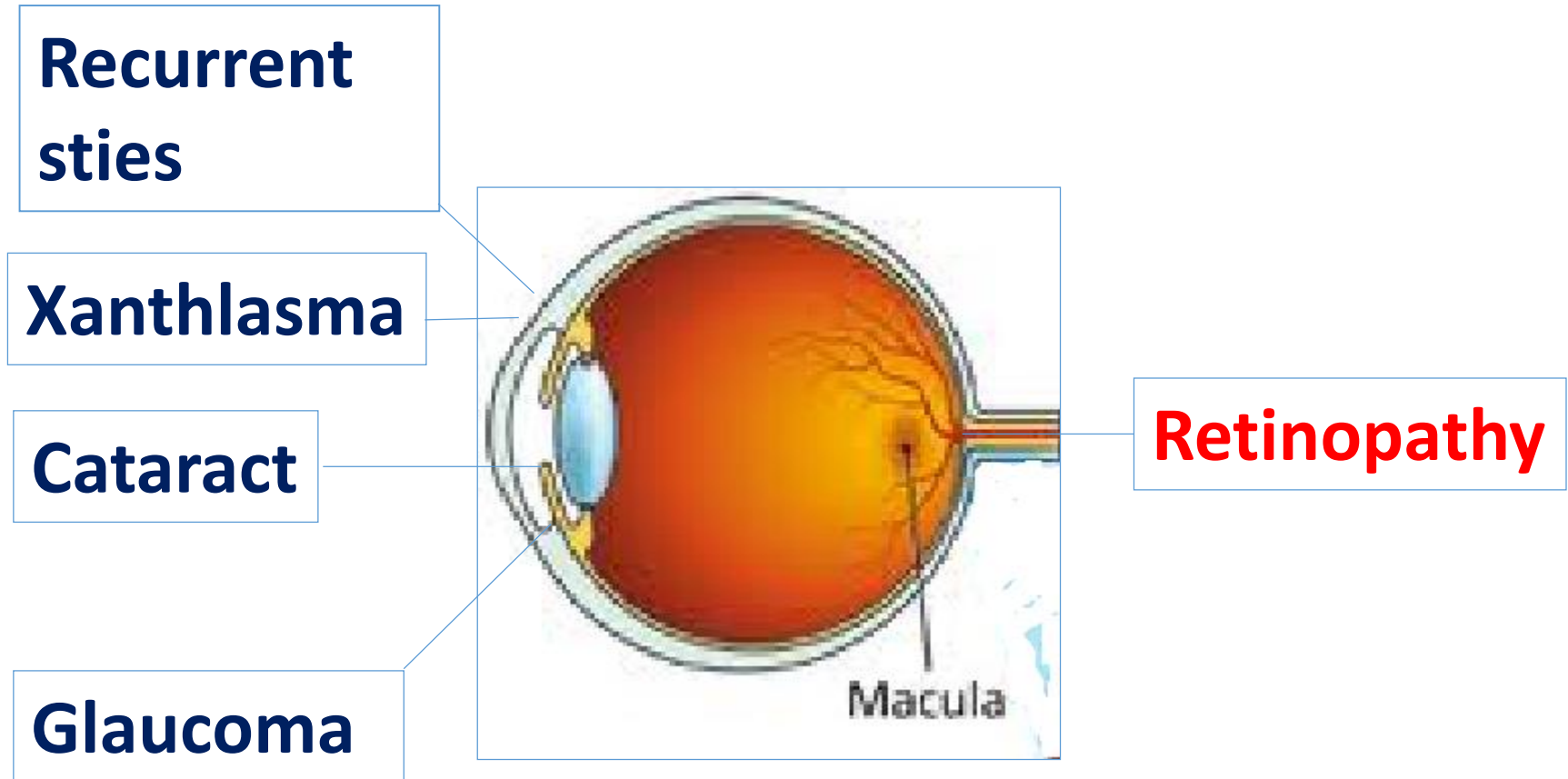
2-Diabetic kidney disease (nephropathy)

3-Diabetic neuropathy

Complications of DM



Diabetic Eye Disease



Diabetic Retinopathy

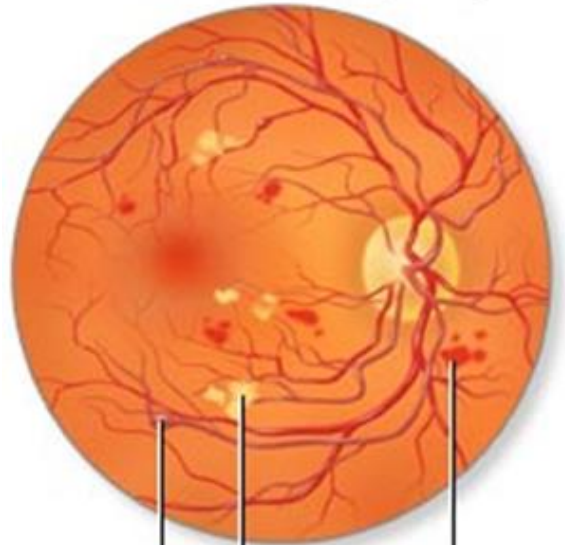
Proliferative retinopathy



Growth of abnormal blood vessels

Early photocoagulation can prevent BLINDNESS!!

Exudative



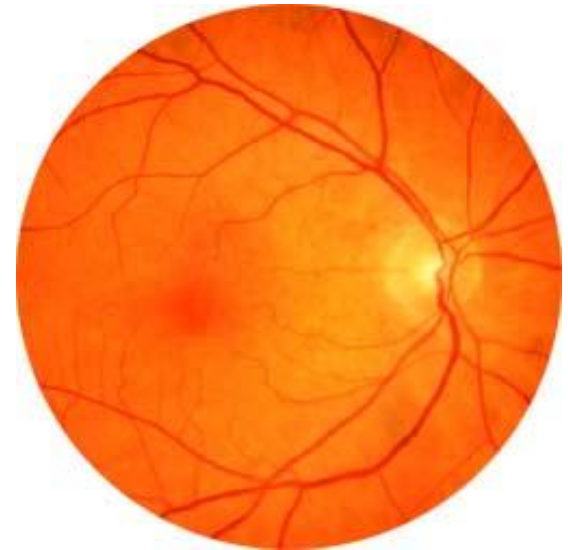
Aneurysm

Hemorrhage

Hard exudate

- 1- **Hard exudates:** Leak of Plasma
- 2- **Cotton Wool exudates:** due to ischemia (ominous sign)

Normal Retina



Diabetic Kidney Disease

① Many factors play a role in the pathogenesis of Diabetic nephropathy.

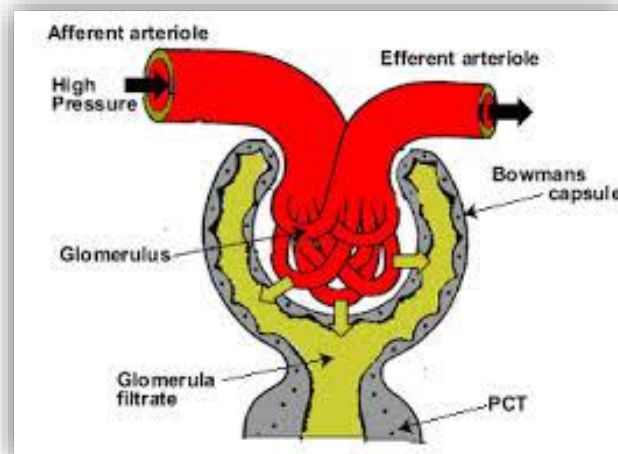
These include:

Hyper-filtration injury (due to  GFR)- Atherosclerosis- Infections- VUR (due to autonomic neuropathy)- and others.

② The condition can range from mild proteinuria to End Stage Renal Failure (ESRF).

(**Proteinuria** is considered to be the main feature of this condition)

③ Early proteinuria could be diminished by the use of **ACE-I**

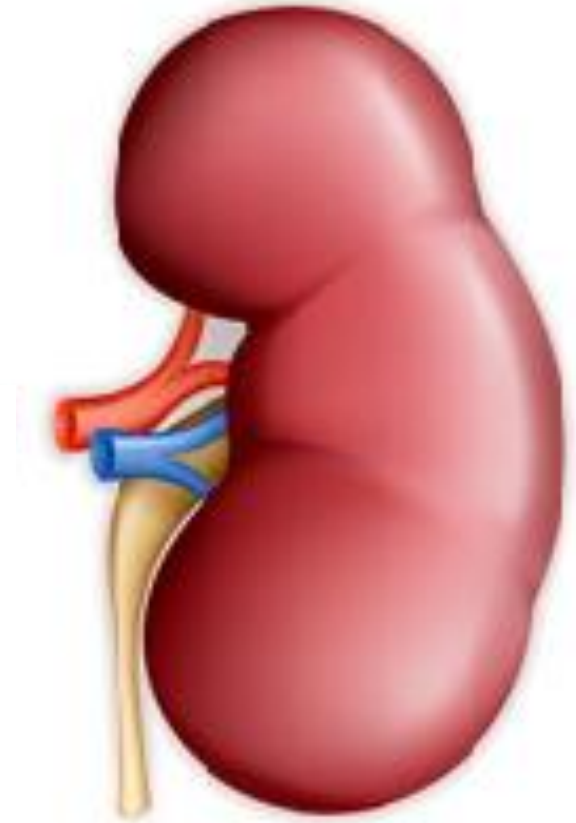


Stage I: Increase GFR-increase kidney size-
micro albuminuria more than
15ug/minute BUT less than 100
ug/minute-NO increase in incidence of
Hypertension.

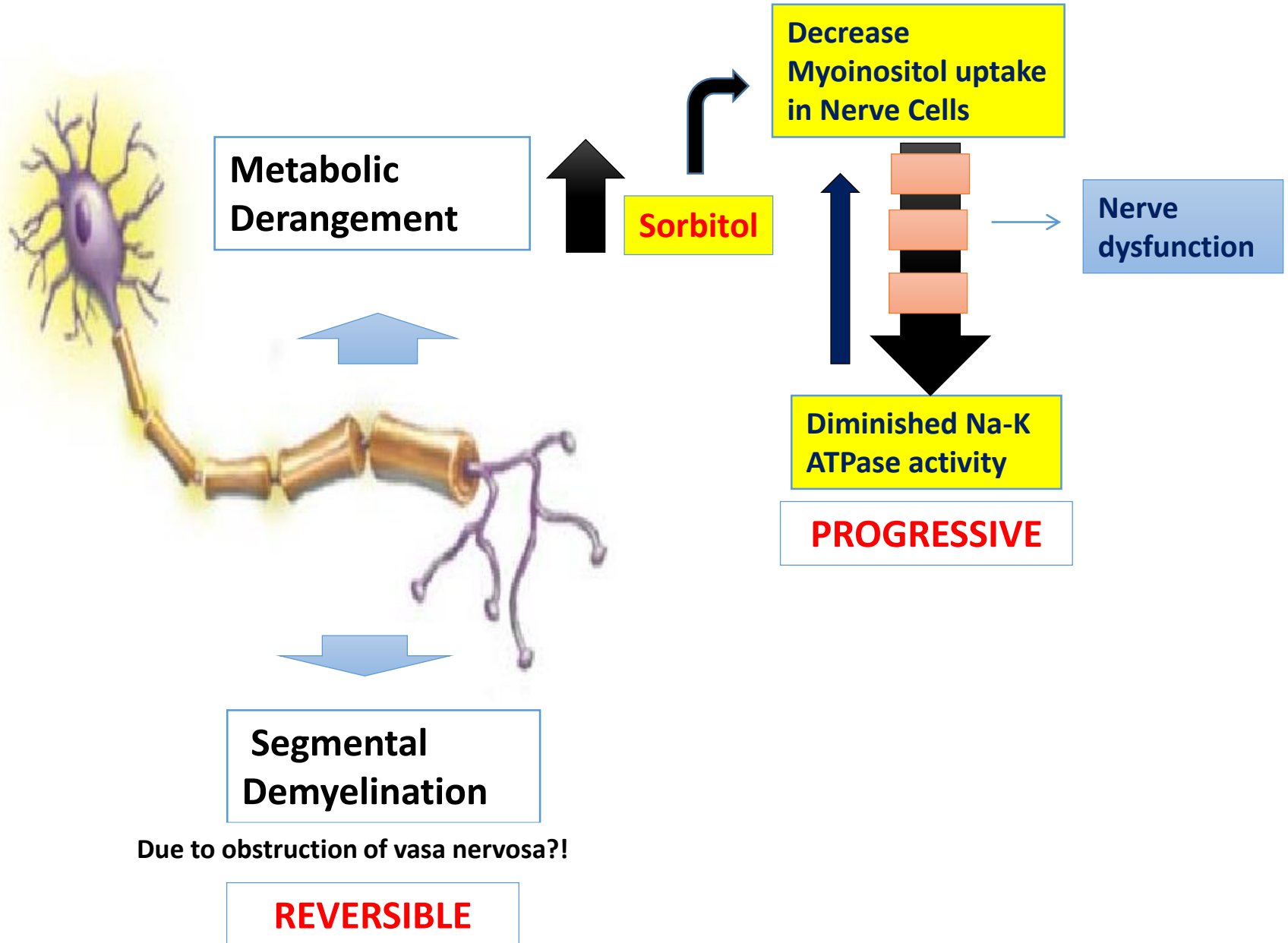
Stage II: Declining GFR-increasing
proteinuria that may reach
nephrotic range within years
(Hypertension and Edema?!)

Stage III: Rapid decrease in GFR that
leads to Azotemia- Hypertension
and oedema worsens...Finally,
Hypoproteinemia and widespread
microangiopathy.

Stage IV: ESRF



Diabetic Neuropathy



① Peripheral neuropathy

① The Most common type

② A generalized sensorimotor

polyneuropathy affecting legs earlier than hands

③ Early loss of tendon reflexes/vibration sense

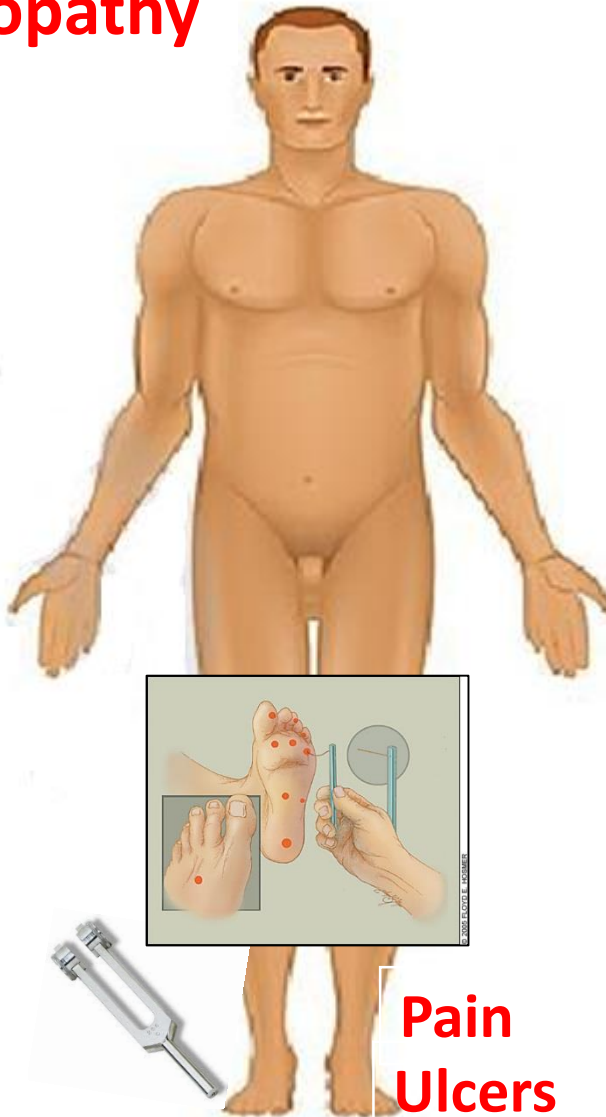
④ Muscle weakness

⑤ May lead to deformities and leg ulcers

⑥ Early detection by Neurothesiometer -for pain threshold

⑦ If severe pain treatment by Amitriptyline/topical capsaicin (depletes substance P) also ?!

Mexiletine



Pain
Ulcers

Early loss of
vibration sense

2 Autonomic Neuropathy

(ttt) by (Stop precipitating drugs-elevate head of the bed-socking-high Na Intake Fludrocortisone)

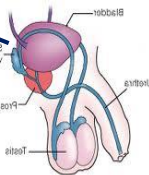
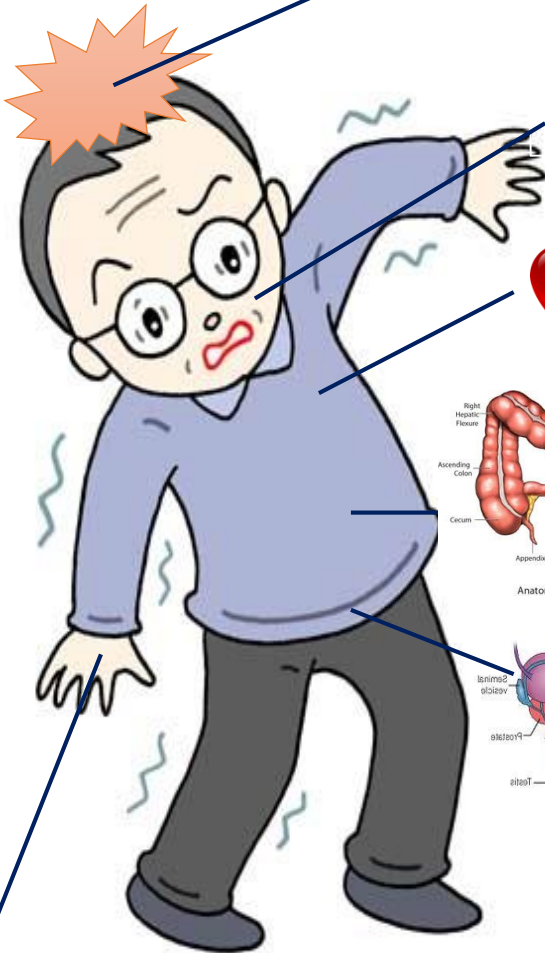
Postural Hypotension

Gustatory sweating

Resting Tachycardia

Constipation/
Diarrhea

Retention of urine....(infections)
Impotence



Loss of RSA

③ Mononeuropathy (or Mononeuropathy Multiplex)

- 1-?!Acute thrombosis or Ischemia of vasa nervosa
- 2-Acute onset neuropathy
- 3-**Reversible within 1-3 MONTHES**
- 4-The commonest site is the 3ed cranial nerve
- 5-If+++++++ pain> insomnia and weigh loss



Reversible

Diabetes Mellitus

Part III (Treatment)



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Treatment of DM

Diet

The following are general recommendations for diabetic patients

Ideal body weight especially by decreasing caloric intake.

Carbohydrate (50%): better complex Carbohydrates.

Fat (35%) with saturated fat $<1/3$

Protein (15%) (substitute poultry, veal, and fish for red meat)

Increase soluble fiber content e.g. beans-oat meals-apple skin.....as they retard nutrient absorption rates thus improve the glycemic control.

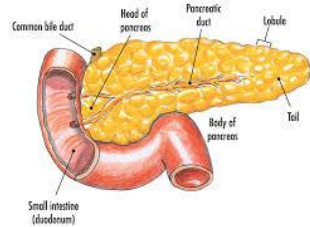
Artificial sweeteners

Moderate regular exercise and increase Carbohydrates before exercise

Treatment of DM

Oral Hypoglycemic Drugs

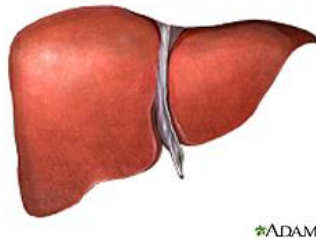
Sulfonylureas



Increase Insulin secretion by beta cells of the pancreas

Hypoglycemia

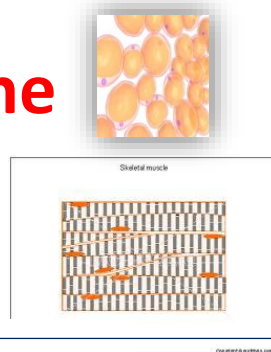
Biguanides



Decrease Hepatic glucose production (useful in Obese patients)

Lactic acidosis

Thiazolidinedione

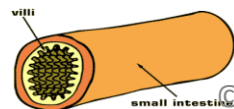


Increase Muscle and adipose tissue glucose uptake

Liver damage

(Monitor the Liver)

Alpha glycosidase inhibitors



Slow carbohydrate absorption

Flatulence

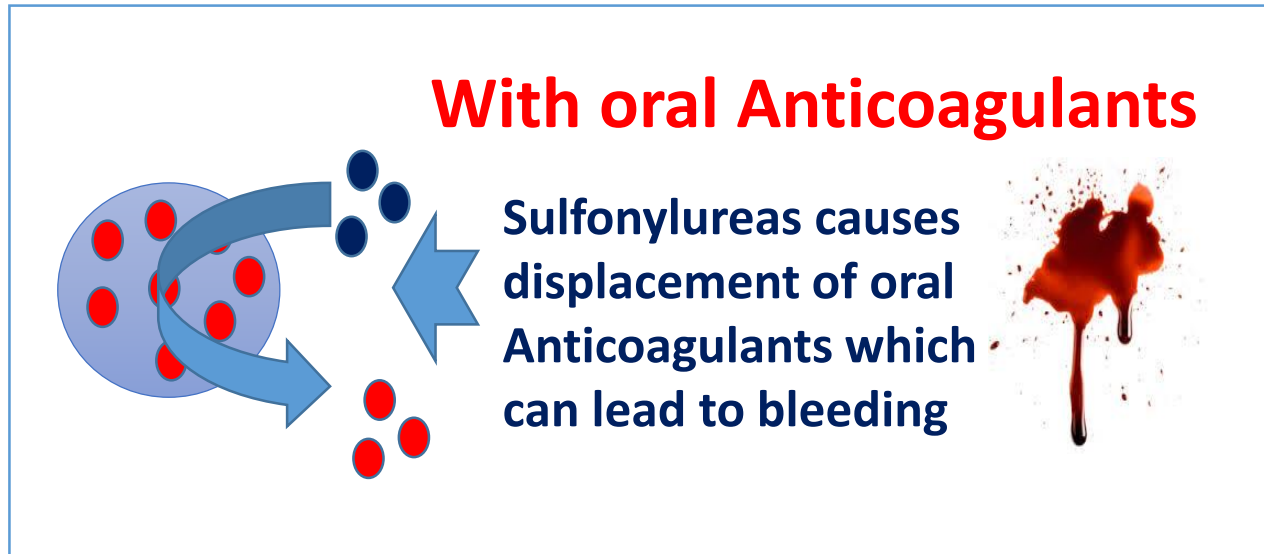
Treatment of DM

Drug interactions of Sulfonylureas [1]



Treatment of DM

Drug interactions of Sulfonylureas [2]



Treatment of DM

Insulin

Indications for using Insulin

- ① **IDDM (Type 1)**
- ② **NIDDM (Type 2) after failure of diet and oral hypoglycemics (i.e. failure to bring FPG below 180 mg/dl)**
- ③ **Pregnancy**
- ④ **Emergency conditions such as Infections-Operations-DKA**

Treatment of DM

Types of Insulin

Onset

Peak

Duration

**Rapidly acting
(Regular
Insulin)**

1H

6h

14h

**Intermediately
acting (NPH)**

1h

10h

24h

**Long acting
(protamine
Zink)**

7h

16h

36h

Treatment of DM

How to use Insulin

- ① Since the response to insulin is individual so we should use **“Trial and error”** approach
- ② **Initial dose is usually 15-20 U** (if the patient is obese 25-30 U due to insulin resistance)...then gradually increase the dose by 5-10 U per step
- ③ **Rotate injection sites** within the same area to avoid lipoatrophy at injection sites But **AVOID** random rotations between different areas to avoid day to day variability.
- ④ If the patient needs to only increase soluble insulin (**Normally: NPH 2/3 + Sol 1/3**) consider mixing problem and shift to separate injections.

Trial and error

**Small initial dose
15-20 U**

Rotate injections



Treatment of DM

How to adjust the Insulin dose

- ① Most people use **two doses of mixed insulin per day** (Sol plus Med acting) (one injection before breakfast and one before dinner)
- ② This gives easier adjustment for blood glucose
- ③ Insulin is given **30 minutes before meals** so that by the time it is absorbed it matches the absorption of food
- ④ Initially you need to measure the patient's blood glucose **4 times a day** (before breakfast-before lunch-before dinner- and before bedtime)
- ⑤ When blood glucose is high at any time you need to **increase the Insulin dose that controls it** e.g. if blood glucose is high in the morning, you need to increase the insulin dose that controls this time of the day (which is by increasing the evening Intermediate acting insulin as its peak of action is after 10 hours i.e. covers the morning blood glucose) [see the illustrations in the next page]

Dose 1

Soluble + IA insulin

Dose 2

**Blood
Glucose**

Morning time

Lunch time

Evening time

Before sleep

**Increase the
evening IA
insulin**

**Increase the
morning
soluble insulin**

**Increase the
morning IA
insulin**

**Increase the
evening
soluble insulin**

Diabetes Mellitus

Part IV (DKA)



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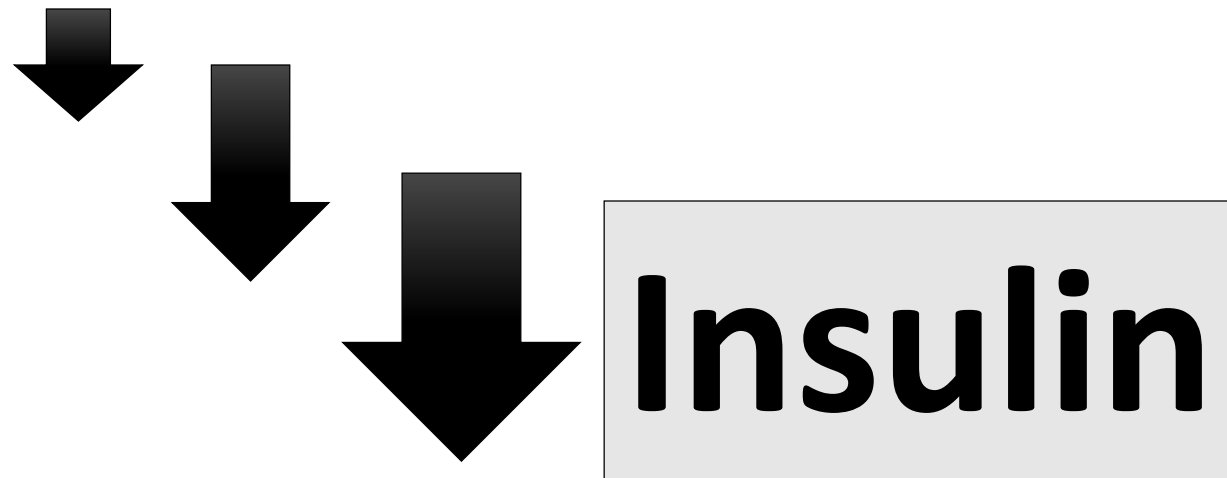
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Diabetic Keto Acidosis DKA

Definition

DKA is a life threatening condition that occurs secondary to severe insulin deficiency.



Diabetic Keto Acidosis DKA

Aetiology



- 1 **Decrease insulin dose**
- 2 **Severe infections** (due to increase anti-insulin antibodies as part of immune reaction against the infection)
- 3 **Type 1 DM**
- 4 **Stress** e.g. AMI-Pancreatitis-Uremia-accidents- and Surgical Operations (due to increase anti-stress hormones which interfere with insulin action).

↓ Insulin

Pathogenesis of DKA

↑ **Glucose**

↑ **Lipolysis**

Ketone bodies

Acidosis

ANV

Deep Rapid Respiration
(Kusmols breathing)

Mental Confusion

Cardiac Contractility

(**Hyperkalemia**)..... ↑



k

Glycosuria

Polyuria

↑ **Hematocrit value**

Loss of electrolytes
Na, K (Total)

Hypovolemic

Shock

Adrenocortical activity

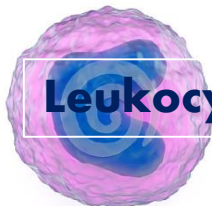
↓ **RBF**

Serum osmolality



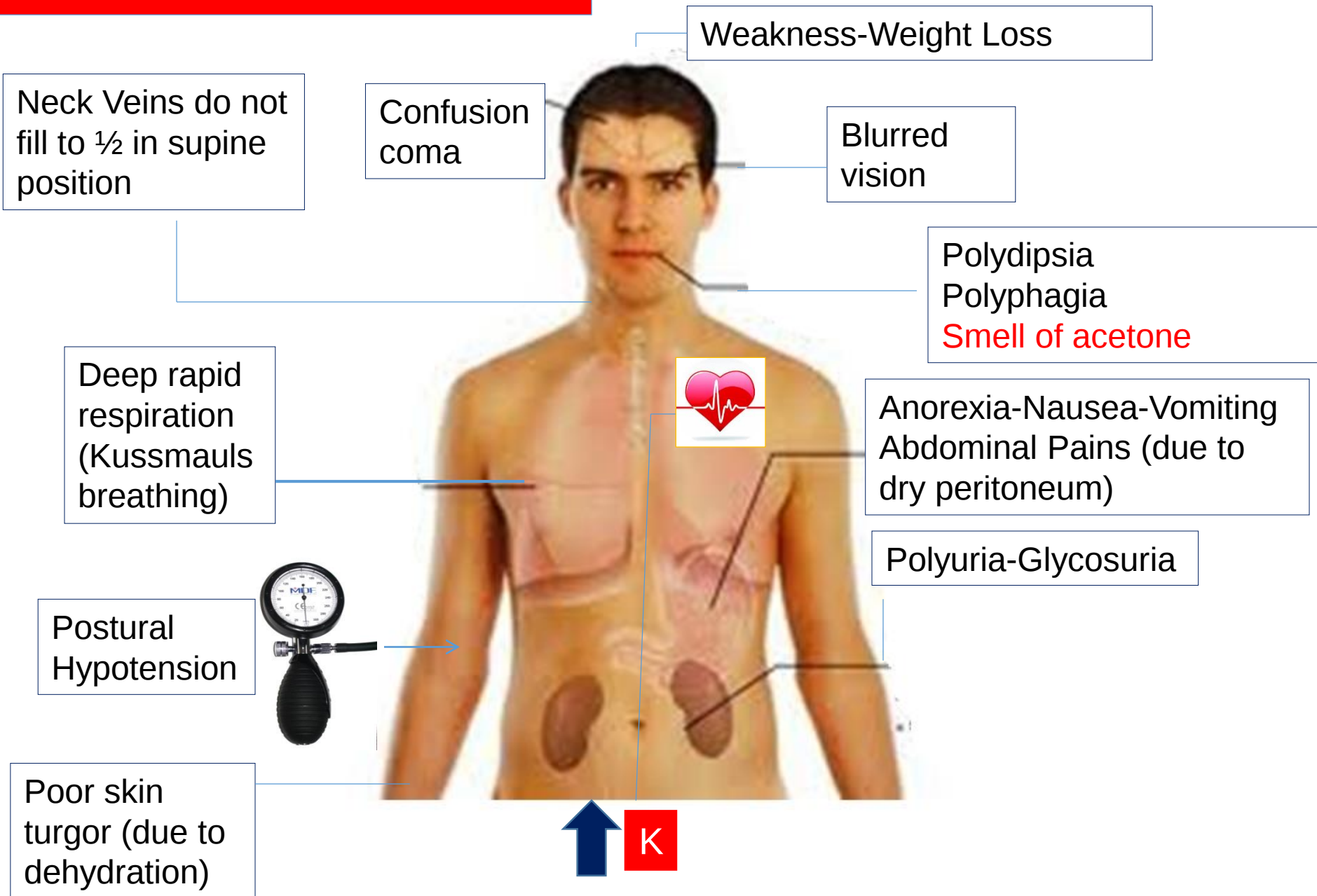
BUN & Creatinine

Leukocytosis



CNS depression

Clinical Manifestations of DKA



Special investigations for DKA

- 1-High blood glucose level (More than 250mg/dl)**
- 2-Acidosis**
- 3-Low serum bicarbonate level**
- 4-Positive ketone bodies in blood**

Note1

Hypovolemic in DKA can present as:

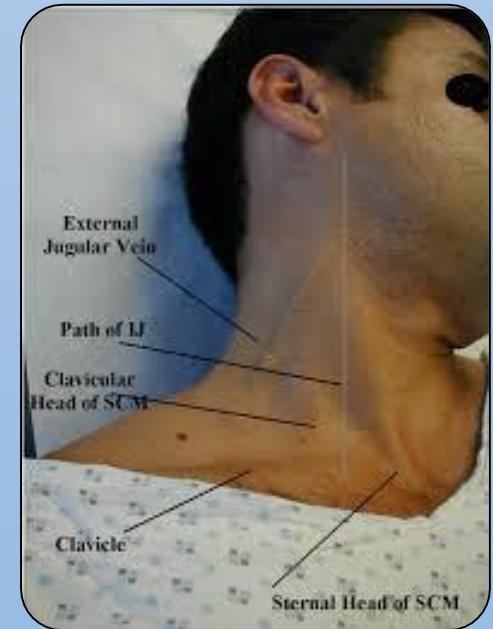
Orthostatic Hypotension

Dry mouth

Abdominal pain

Poor Skin turgor

Failure to fill the jugular veins to its 1/2 while the patient is supine



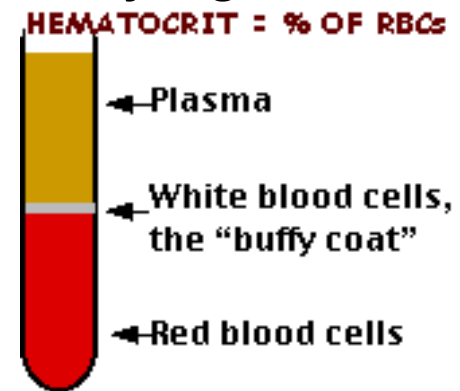
Note 2

Since **Hematocrit values is typically high in DKA** (due to loss of water in polyuria), accordingly the presence of NORMAL Hematocrit in patients with DKA may indicate the presence of underlying anemia.

Normal Hematocrit in DKA

=

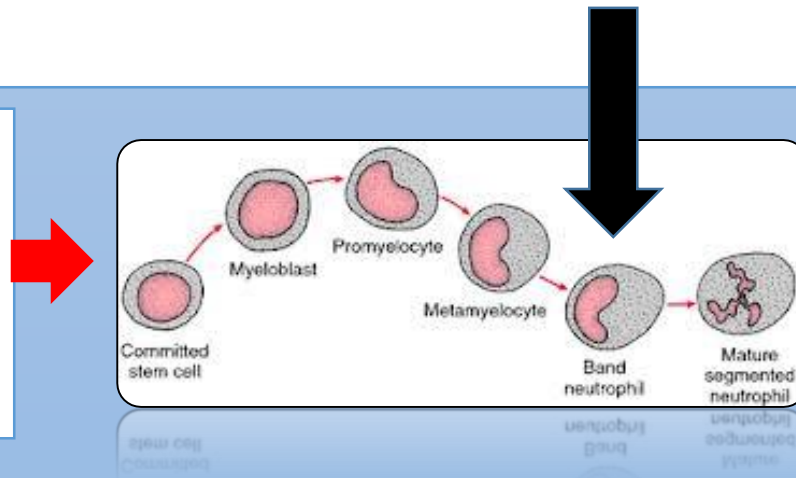
?!Anemia



Note 3

Leukocytosis associated with DKA is typically associated with : **No increase in band neutrophils.** If Band Neutrophils were increased....You should suspect infection.

Infection
Increases
Band
Neutrophils.



The dilemma of K in DKA

k

Serum K is 5 units

5

5

Normal situation

Total K is 10 Unites

DKA

1

7

In DKA the **total K** is low but **serum K** is high

Serum K is 7 units

Total K is 8 Unites
(due to loss in urine)

Treatment of DKA

1-Soluble Insulin IV to correct the hyperglycemia

2-Saline Infusion to correct the hypovolemic

3-K infusion to correct the total K deficit (but take care to give it ONLY with or after Insulin to avoid marked hyperkalemia (as serum K is already high due to the presence of acidosis)

4-Correction of any predisposing factors e.g. ttt of associated infection by antibiotics

5-ttt of complications e.g. Acidosis- Low PO₄- others

Insulin

Saline

**K ONLY
after
Insulin**

**ttt of
associated
infection**

**ttt of
acidosis (if
needed**

Note:



**Bicarbonate is used ONLY if PH
is less than 7.1**

**Mild acidosis is usually
corrected after giving
insulin as the acid radicals
are metabolized.**

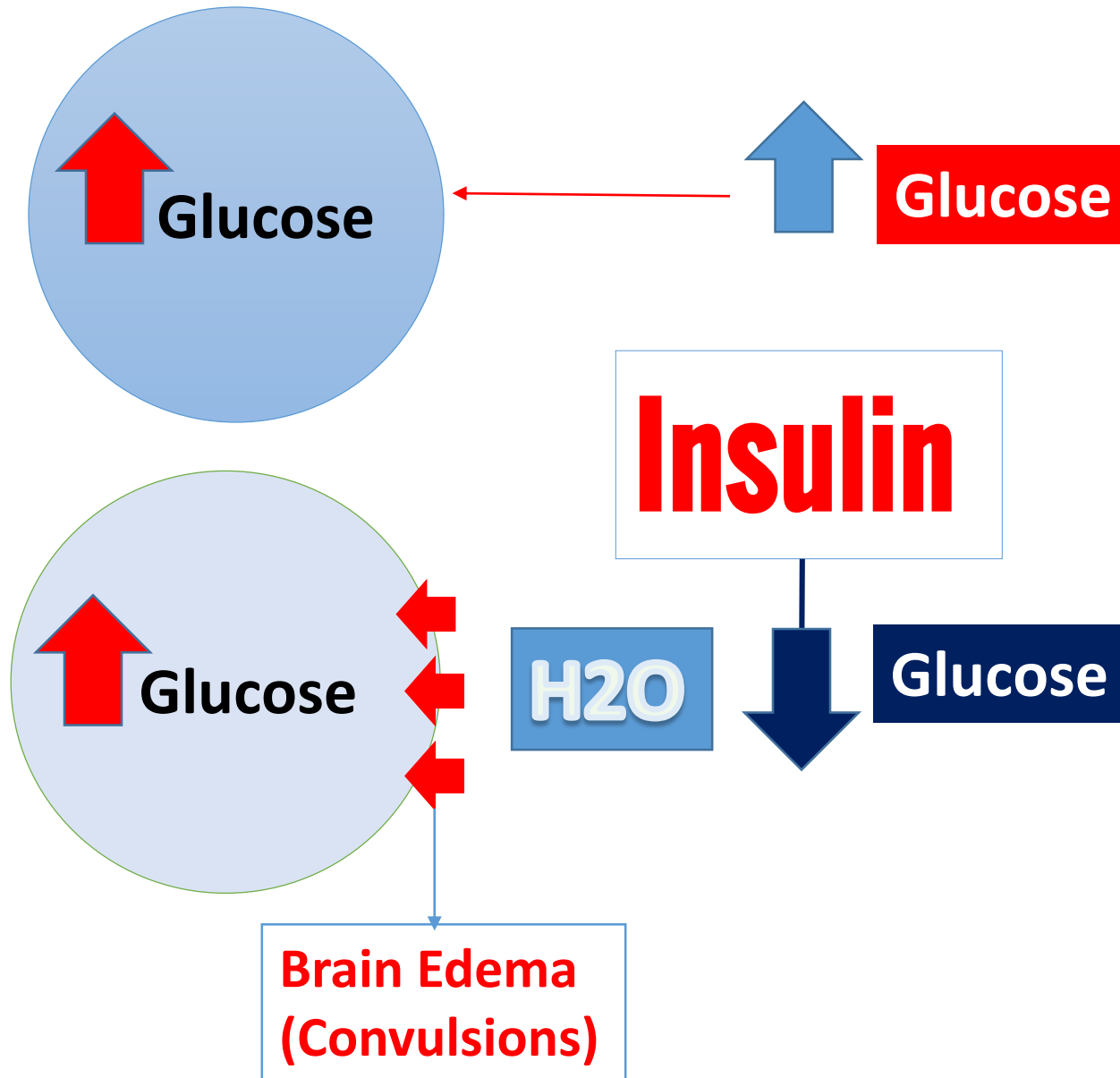
Saline infusion



① 0.9% Saline infusion 1L/h for the first 2 hours then ½ L/h.

② When blood glucose level is lowered to 250 mg/dl change the fluid to 5% glucose containing solution to prevent Hypoglycemia and brain edema (due to disequibration syndrome).

Disequilibration syndrome



Insulin



Start by 0.15 unit/Kg as an IV bolus to prime the tissues insulin receptors then give 0.1 unit/kg/h as continuous infusion or IM injection

K



If the patient is not uremic and has an adequate urinary output KCl 10-30 mEq/h is given 2-3 hours **AFTER** Insulin



**Tomato
Juice**



Banana

Bicarbonate

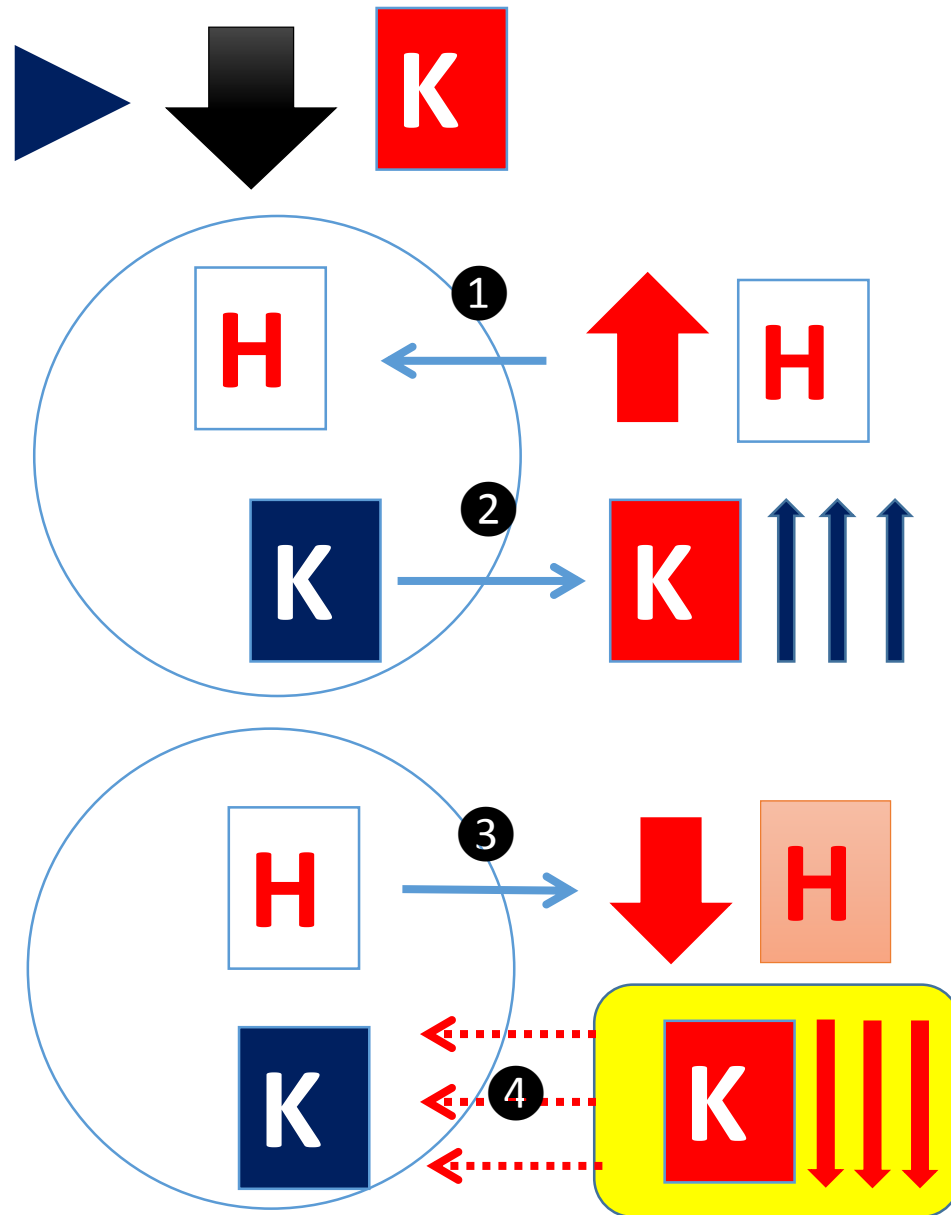


Only if PH less than 7.0

One or two ampules of Na Bicarbonate should be added to 1L of 0.45% saline.

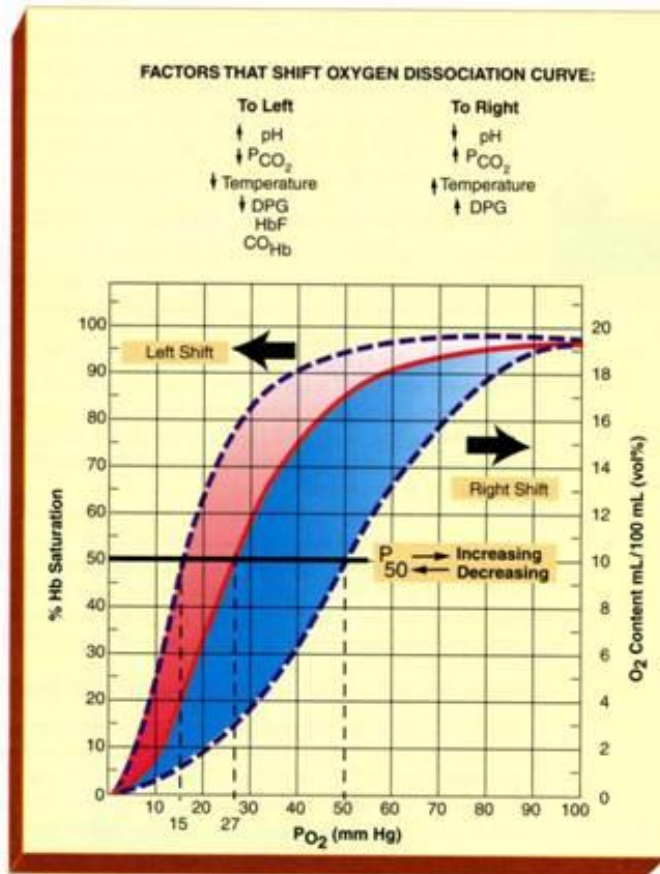
Avoid adding Na Bicarbonate to 0.9% saline as this will lead to the creation of markedly hypertonic solution which will aggravate the hyperosmolar state.

Complications of Bicarbonate therapy [1]



Complications of Bicarbonate therapy [2]

Tissue Hypoxia



Impair
Oxygen
delivery to
tissues

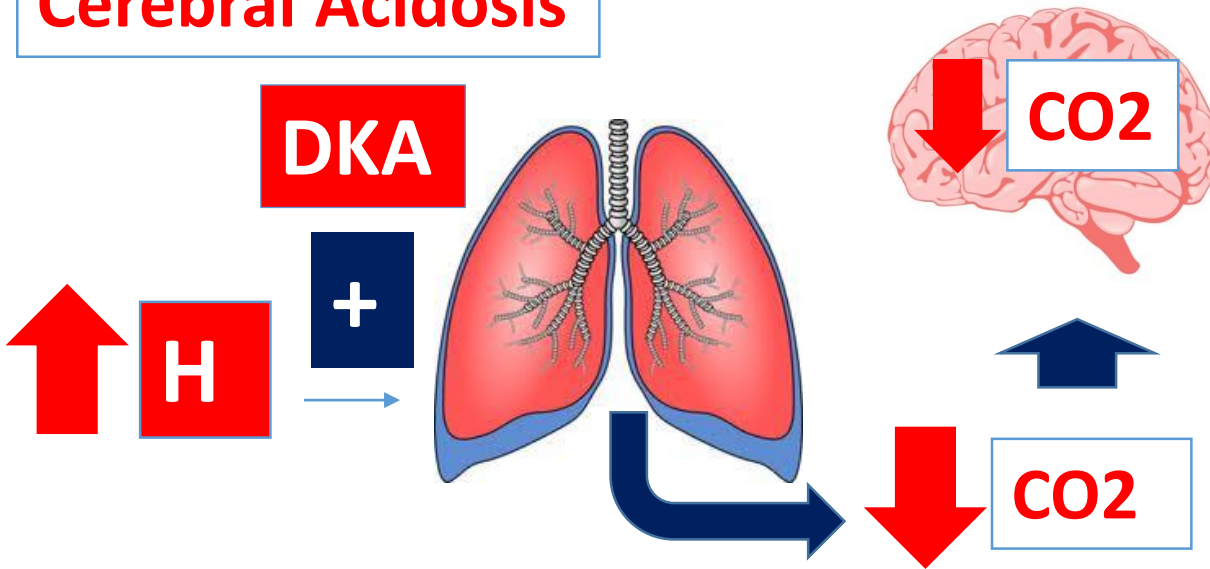
+

Shock

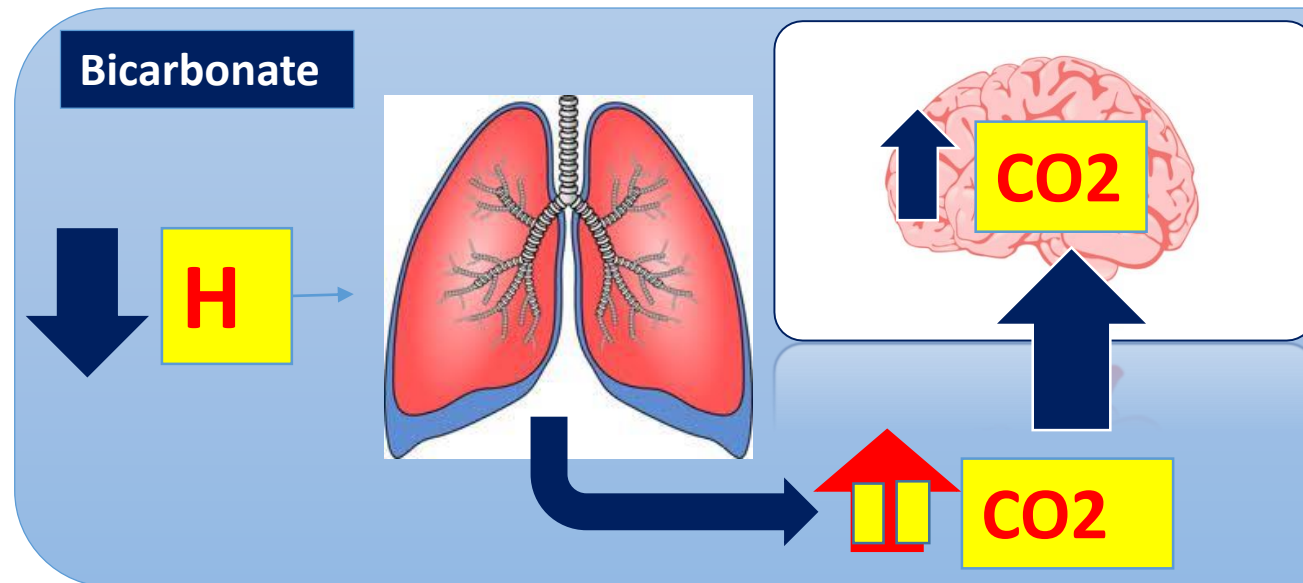
Shift to the Left

Complications of Bicarbonate therapy [3]

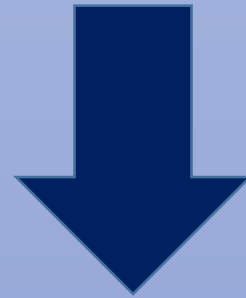
Cerebral Acidosis



Bicarbonate



After insulin therapy the body tries to build its own denatured proteins...this utilizes PO4 and may cause Hypophosphatemia that manifests as severe **Muscle Weakness** which may need treatment by PO4.



PO4

Hypoxia

Ketone bodies

Beta-OH-
Butyrate (Un-
measurable)

NADH+H

NAD

Acetoacetate
(measurable)

If severe tissue hypoxia developed as a result of the Shock in cases of DKA, NADH+H and consequently beta OH-Butyrate increases (at the expense of NAD and Acetoacetate). This may lead to a decline in Ketone body measurements (as beta OH butyrate is usually UNMEASUSABLE) despite worsening of the clinical situation. Accordingly, observing the **clinical condition and PH** of the patient in DKA is probably more important than measuring ketone bodies.

Diabetes Mellitus

Part V (Hypoglycemia, HONKS, Others)



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تحذير هام

هذا الفيديو و جميع الرسوم التوضيحية المتاحة فى هذا الموقع هم تحت حماية قانون الملكية الفكرية

هذا الفيديو و جميع الرسوم التوضيحية المتاحة فى هذا الموقع هم تحت حماية قانون الملكية الفكرية و لا يحق لأحد إستخدامه أو إستنساخه أو إعادة طبعه أو طبع أجزاء منه بدون إذن مسبق من الدكتور طارق عبد الحميد (أو من ينوب عنه قانونياً). و من يتعدى على الملكية الفكرية المذكورة فسوف يتعرض للمسائلة القضائية عن جريمة إنتهاك حقوق الملكية الفكرية. و إستخدام الفيديوهات و المادة العلمية المذكورة مكفول فقط لمشترى واحد فقط و لأخذ تصريح إستخدام لأكثر من شخص برجاء الإتصال بالدكتور طارق عبد الحميد



Hypoglycemia

Definition

A Metabolic Syndrome caused by severe by hypoglycemia in diabetic patients

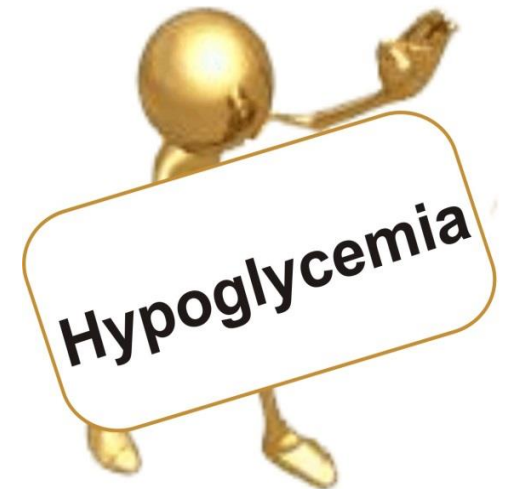


Glucose

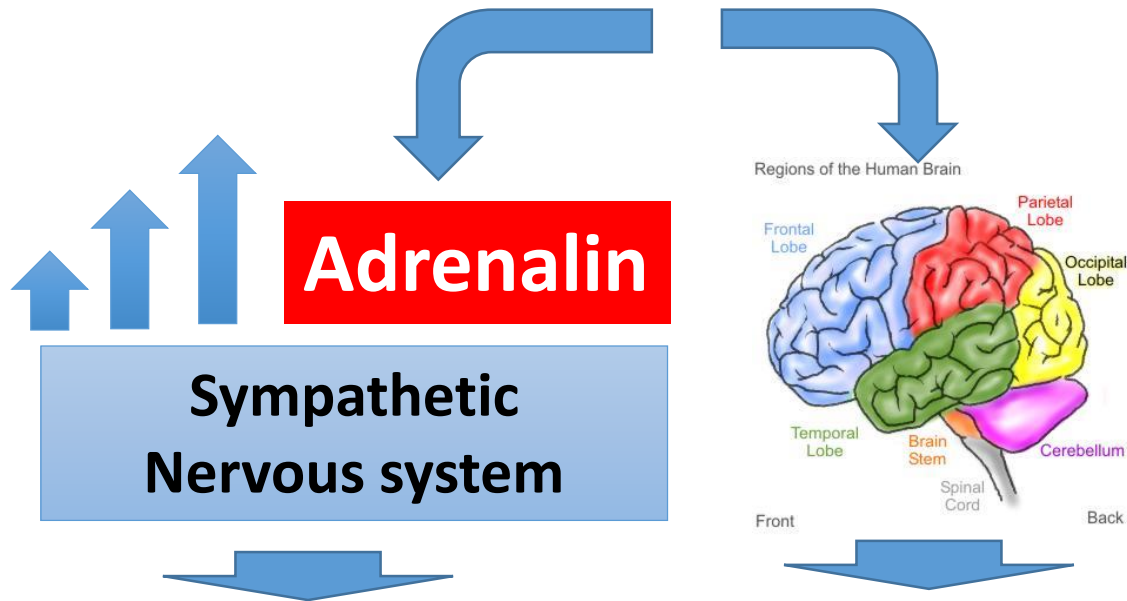
Aetiology

Predisposing factors for the development of hypoglycemia in a diabetic patient include:

- 1- Overdose of Insulin or Sulfonylurea**
- 2- Lacking a Meal after insulin injection**
- 3- Severe exercise after insulin injection (as this may increase the rate of insulin absorption from the injection site)**



GLUCOSE



Adrenalin

**Sympathetic
Nervous system**

**Low serum glucose
level (usually less
than 60 mg/dl)**

Sweating
Palpitation
HR
Tremors
Irritability
Nervousness
Hunger pains

Visual disturbance
Confusion
Headache
Abnormal behavioral
Convulsions
Coma with Hyperreflexia
(due to dysfunction of the
pyramidal tract)

Mental confusion

Headache

Visual disturbances

excessive sweating

Tremors

Palpitation

Hunger Pains

Increase Reflexes



Coma

Treatment of Hypoglycemia

IV 50% 50 CC Glucose

or/

IM Glucagon 1mg IM

or/

Oral Glucose (if the patient is conscious)

Note



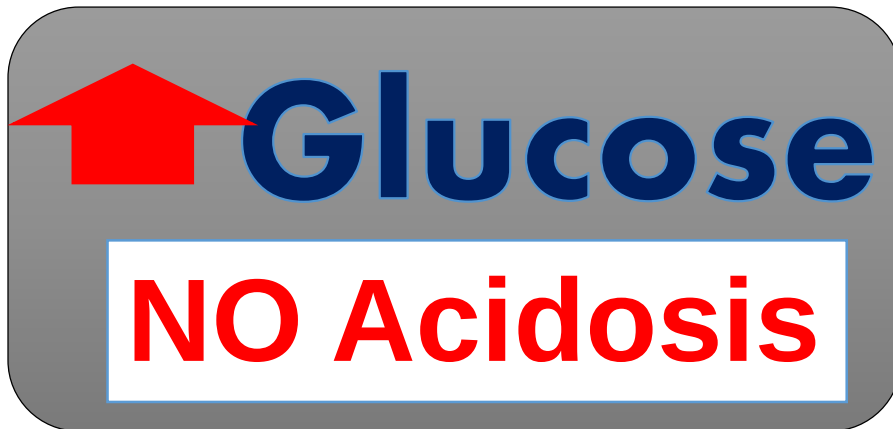
The treatment should be followed by an **ORAL snack** to replenish hepatic glycogen and thus prevent recurrence of Hypoglycemia.



Hyperosmolar Non-Ketotic Syndrome

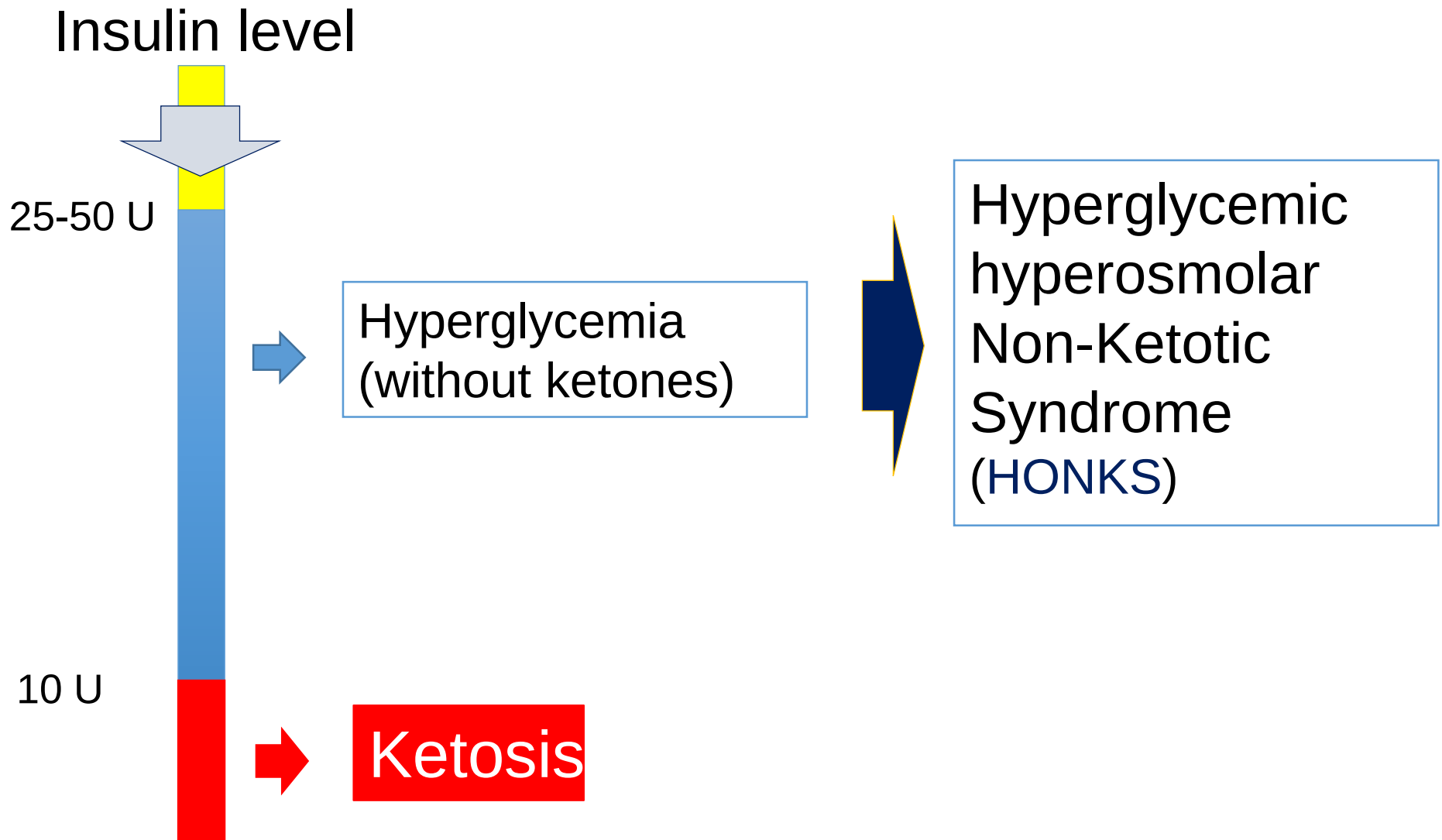
Definition

Marked increase in serum osmolality in a diabetic patient WITHOUT associated acidosis.



Aetiology of HONKS

Insulin deficiency



Pathogenesis of HONKS

1-Same pathophysiology as DKA except that serum insulin levels are not low enough to cause ketosis.

2-Since **ketosis is absent**, anorexia and vomiting are NOT typically present

3-The lack of vomiting makes the patient late in seeking medical advice....this delay causes:

① Higher glucose concentration on initial measurements

② Higher serum osmolality: this can cause more focal neurological signs than DKA

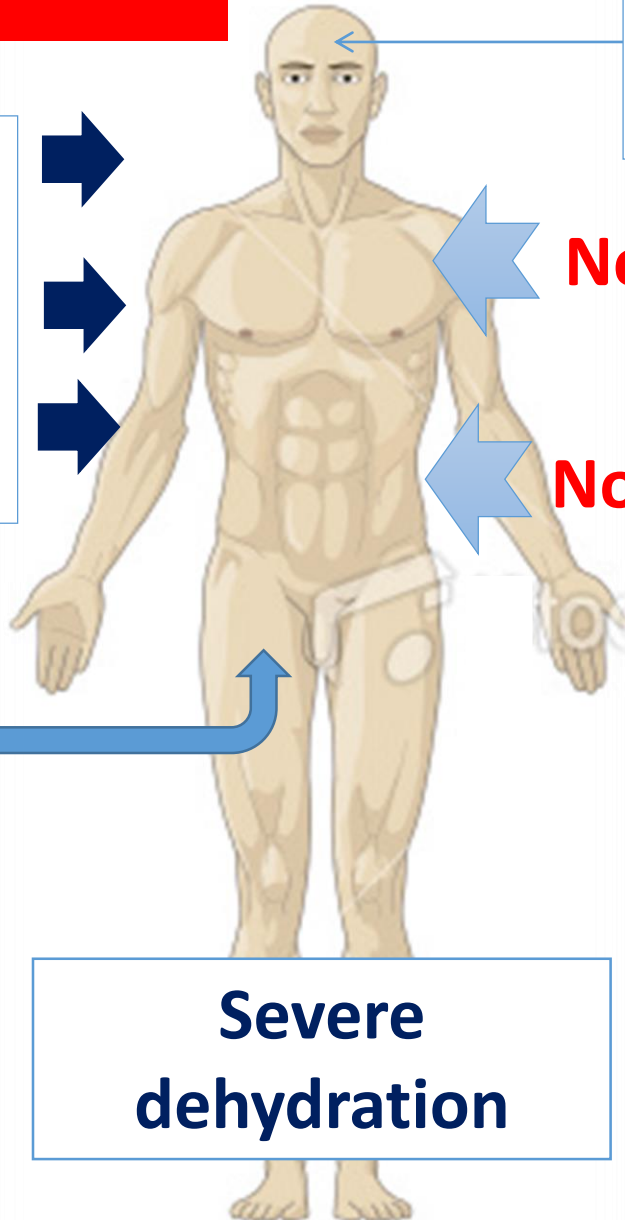
③ More severe dehydration

The last 3 points explain to us why and how HONKS have higher mortality rate than DKA!

Clinical picture

Preceded by
polyuria and
polydipsia
secondary to insulin
deficiency

Muscle
weakness



Focal neurological
signs

No Kussmols breathing

No anorexia or Vomiting

Severe
dehydration

Special investigations for HONKS

- 1 Hyperglycemia: More than 600 mg/dl
- 2 High serum osmolality (More than 310 mosm/kg)
- 3 No acidosis (except if complicated by shock as the latter may cause hypoxia which may result in Lactic acidosis)

Treatment of HONKS

Saline

Insulin

K

Management of complications of DM (1)

Severe vomiting



Check for DKA

Diabetic diarrhea



**Empirical antibiotic
therapy e.g.
tetracycline
cephalosporin**

**Erectile
dysfunction**



Sildenafil (NEVER** use
it with nitrates as this
can cause fatal
hypotension)**

Management of complications of DM (2)

Slaw gastric emptying



Metoclopramide (Note: my cause extrapyramidal manifestations due to its anti dopaminergic action)

Painful neuropathy



Amitriptyline

Retinopathy



Photocoagulation

Management of complications of DM (3)

**Orthostatic
Hypotension**



- 1 Compressive garments**
- 2 NaCl**
- 3 Fludrocortisone**

**Nephropathy and
High BP**



**ACEI (as it decreases
micro albuminuria)**